

**AMENDMENT**

Kindly amend the application, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

**IN THE CLAIMS:**

Kindly amend the claims, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, to read as follows:

1. (Currently Amended) An isolated polypeptide comprising an extracellular domain as recited in SEQ ID NO: 22, which polypeptide:

- i) comprises or consists of the amino acid sequence as recited in SEQ ID NO:16 or SEQ ID NO:26; or
- ii) consists of the amino acid sequence as recited in SEQ ID NO:20 or SEQ ID NO:22 or ~~consists of a combination of the amino acid sequences as recited in SEQ ID NO:4 and SEQ ID NO:6; or~~
- iii) is a fusion protein comprising a polypeptide according to i) or ii) or comprising a fragment of a polypeptide according to i) or ii) fused to a heterologous polypeptide; or
- iv) is a functional equivalent of (i) or (ii) or (iii), characterised in that it is homologous to the amino acid sequence as recited in SEQ ID NO:16 or SEQ ID NO:26 and has activity as an antagonist of cytokine expression and/or secretion.

2-3. (Cancelled)

4. (Withdrawn) A purified nucleic acid molecule which encodes a polypeptide according to claim 1.

5. (Withdrawn) A purified nucleic acid molecule according to claim 4, which comprises the nucleic acid sequence as recited in SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:25, or is a redundant equivalent or fragment thereof.

6. (Withdrawn) A purified nucleic acid molecule according to claim 5, which consists of the nucleic acid sequence as recited in SEQ ID NO:15, SEQ ID NO:19, SEQ ID NO:21 or SEQ ID NO:25.

7. (Withdrawn) A purified nucleic acid molecule which hybridizes under high stringency conditions with a nucleic acid molecule according to claim 4.
8. (Withdrawn) A vector comprising a nucleic acid molecule as recited in claim 4.
9. (Withdrawn) A host cell transformed with a vector according to claim 8.
10. (Currently Amended) An isolated ligand which binds specifically to, and which preferably inhibits the activity of a polypeptide of claim 1.
11. (Previously Presented) An isolated ligand according to claim 10, which is an antibody.
12. (Previously Presented) A compound that either increases or decreases the level of expression or activity of a polypeptide according to claim 1, compared to the level of expression or activity of the polypeptide in the absence of the compound.
13. (Previously Presented) A compound that either increases or decreases the level of expression or activity of a polypeptide according to claim 1, relative to the level of expression or activity of the polypeptide in the absence of the compound, wherein the compound binds to a polypeptide according to claim 1 without inducing any of the biological effects of the polypeptide.
14. (Previously Presented) A compound according to claim 13, which is a natural or modified substrate, ligand, enzyme, receptor or structural or functional mimetic.
15. (Previously Presented) An isolated polypeptide according to claim 1 for use in therapy or diagnosis of an inflammatory disease, an autoimmune disease, liver disease, or liver failure.
16. (Cancelled)
17. (Withdrawn) A nucleic acid molecule according to claim 4 for use in therapy or diagnosis of disease.
18. (Withdrawn) A vector according to claim 8 for use in therapy or diagnosis of disease.
19. (Withdrawn) A host cell according to claim 9 for use in therapy or diagnosis of disease.
20. (Previously Presented) A ligand according to claim 10 for use in therapy or diagnosis of an inflammatory disease, an autoimmune disease, liver disease, or liver failure.

21. (Previously Presented) A compound according to claim 12 for use in therapy or diagnosis of an inflammatory disease, an autoimmune disease, liver disease, or liver failure.

22. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to claim 1, or assessing the activity of a polypeptide according to claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease.

23. (Withdrawn) A method according to claim 22 that is carried out in vitro.

24. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to claim 1, or assessing the activity of a polypeptide according to claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, which comprises the steps of: (a) contacting a ligand which binds specifically to, and which preferably inhibits the activity of a polypeptide according to claim 1 with a biological sample under conditions suitable for the formation of a ligand-polypeptide complex; and (b) detecting said complex.

25. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to claim 1, or assessing the activity of a polypeptide according to claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, comprising the steps of:

a) contacting a sample of tissue from the patient with a nucleic acid probe under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule which encodes a polypeptide according to claim 1 and the probe;

b) contacting a control sample with said probe under the same conditions used in step a); and

c) detecting the presence of hybrid complexes in said samples; wherein detection of levels of the hybrid complex in the patient sample that differ from levels of the hybrid complex in the control sample is indicative of disease.

26. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to claim 1, or assessing the activity of a polypeptide according to claim 1, in tissue from said patient and

comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, that is carried out in vitro, comprising:

- a) contacting a sample of nucleic acid from tissue of the patient with a nucleic acid primer under stringent conditions that allow the formation of a hybrid complex between a nucleic acid molecule which encodes a polypeptide according to claim 1 and the primer;
- b) contacting a control sample with said primer under the same conditions used in step a); and
- c) amplifying the sampled nucleic acid; and
- d) detecting the level of amplified nucleic acid from both patient and control samples; wherein detection of levels of the amplified nucleic acid in the patient sample that differ significantly from levels of the amplified nucleic acid in the control sample is indicative of disease.

27. (Withdrawn) A method of diagnosing a disease in a patient, comprising assessing the level of expression of a natural gene encoding a polypeptide according to claim 1, or assessing the activity of a polypeptide according to claim 1, in tissue from said patient and comparing said level of expression or activity to a control level, wherein a level that is different to said control level is indicative of disease, that is carried out in vitro, comprising:

- a) obtaining a tissue sample from a patient being tested for disease;
- b) isolating a nucleic acid molecule which encodes a polypeptide according to claim 1 from said tissue sample; and
- c) diagnosing the patient for disease by detecting the presence of a mutation which is associated with disease in the nucleic acid molecule as an indication of the disease.

28. (Withdrawn) The method of claim 27, further comprising amplifying the nucleic acid molecule to form an amplified product and detecting the presence or absence of a mutation in the amplified product.

29. (Withdrawn) The method of claim 27, wherein the presence or absence of the mutation in the patient is detected by contacting said nucleic acid molecule with a nucleic acid probe that hybridises to said nucleic acid molecule under stringent conditions to form a hybrid double-stranded molecule, the hybrid double-stranded molecule having an unhybridised portion of the nucleic acid probe strand at any portion corresponding to a mutation associated with

disease; and detecting the presence or absence of an unhybridised portion of the probe strand as an indication of the presence or absence of a disease-associated mutation.

30. (Withdrawn) A method according to claim 22, wherein said disease is an auto-immune, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

31. (Withdrawn) A method of using a polypeptide according to claim 1 as an antagonist of cytokine expression and/or secretion.

32. (Withdrawn) A pharmaceutical composition comprising a polypeptide according to claim 1.

33. (Withdrawn) A pharmaceutical composition comprising a nucleic acid molecule according to claim 4.

34. (Withdrawn) A pharmaceutical composition comprising a vector according to claim 8.

35. (Withdrawn) A pharmaceutical composition comprising a host cell according to claim 9.

36. (Withdrawn) A pharmaceutical composition comprising a ligand according to claim 10.

37. (Withdrawn) A pharmaceutical composition comprising a compound according to claim 12.

38. (Withdrawn) A vaccine composition comprising a polypeptide according to claim 1.

39. (Withdrawn) A vaccine composition comprising a nucleic acid molecule according to claim 4.

40. (Withdrawn) A method of using a polypeptide according to claim 1 in the manufacture of a medicament for the treatment of an auto-immune disease, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

41. (Withdrawn) A method of using nucleic acid molecule according to claim 4 in the manufacture of a medicament for the treatment of an auto-immune disease, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

42. (Withdrawn) A method of using a vector according to claim 8 in the manufacture of a medicament for the treatment of an auto-immune disease, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

43. (Withdrawn) A method of using a host cell according to claim 9, in the manufacture of a medicament for the treatment of an auto-immune disease, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

44. (Withdrawn) A method of using a ligand according to claim 10 in the manufacture of a medicament for the treatment of an auto-immune disease, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

45. (Withdrawn) A method of using a compound according to claim 12 in the manufacture of a medicament for the treatment of an auto-immune disease, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

46. (Withdrawn) A method of using a pharmaceutical composition of claim 32 in the manufacture of a medicament for the treatment of an auto-immune disease, viral or acute liver disease, including alcoholic liver failure, or inflammatory disease.

47. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a polypeptide according to claim 1.

48. (Withdrawn) A method according to claim 47, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide administered to the patient is an agonist.

49. (Withdrawn) A method according to claim 47, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the polypeptide administered to the patient is an antagonist.

50. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a nucleic acid molecule according to claim 4.

51. (Withdrawn) A method according to claim 50, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the nucleic acid molecule administered to the patient is an agonist.

52. (Withdrawn) A method according to claim 50, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when

compared to the level of expression or activity in a healthy patient, the nucleic acid molecule administered to the patient is an antagonist.

53. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a vector according to claim 8.

54. (Withdrawn) A method according to claim 53, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the vector administered to the patient is an agonist.

55. (Withdrawn) A method according to claim 53, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the vector administered to the patient is an antagonist.

56. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a host cell according to claim 9.

57. (Withdrawn) A method according to claim 56, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the host cell administered to the patient is an agonist.

58. (Withdrawn) A method according to claim 56, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the host cell administered to the patient is an antagonist.

59. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a ligand according to claim 10.

60. (Withdrawn) A method according to claim 59, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the ligand administered to the patient is an agonist.

61. (Withdrawn) A method according to claim 59, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when

compared to the level of expression or activity in a healthy patient, the ligand administered to the patient is an antagonist.

62. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a compound according to claim 12.

63. (Withdrawn) A method according to claim 62, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the compound administered to the patient is an agonist.

64. (Withdrawn) A method according to claim 62, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the compound administered to the patient is an antagonist.

65. (Withdrawn) A method of treating a disease in a patient, comprising administering to the patient a pharmaceutical composition of claim 66.

66. (Withdrawn) A method according to claim 65, wherein, for diseases in which the expression of the natural gene or the activity of the polypeptide is lower in a diseased patient when compared to the level of expression or activity in a healthy patient, the composition administered to the patient is an agonist.

67. (Withdrawn) A method according to claim 65, wherein, for diseases in which the expression of the natural gene or activity of the polypeptide is higher in a diseased patient when compared to the level of expression or activity in a healthy patient, the composition administered to the patient is an antagonist.

68. (Withdrawn) A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression or activity of a polypeptide according to claim 1 in tissue from said patient, wherein altering said level of expression or activity over the period of time towards a control level is indicative of regression of said disease.

69. (Withdrawn) A method of monitoring the therapeutic treatment of disease in a patient, comprising monitoring over a period of time the level of expression of a nucleic acid molecule according to claim 4 in tissue from said patient, wherein altering said level of

expression or activity over the period of time towards a control level is indicative of regression of said disease.

70. (Withdrawn) A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a polypeptide according to claim 1 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.

71. (Withdrawn) A method for the identification of a compound that is effective in the treatment and/or diagnosis of disease, comprising contacting a nucleic acid molecule according to claim 4 with one or more compounds suspected of possessing binding affinity for said polypeptide or nucleic acid molecule, and selecting a compound that binds specifically to said nucleic acid molecule or polypeptide.

72. (Withdrawn) A kit useful for diagnosing disease comprising a first container containing a nucleic acid probe that hybridises under stringent conditions with a nucleic acid molecule according to claim 4; a second container containing primers useful for amplifying said nucleic acid molecule; and instructions for using the probe and primers for facilitating the diagnosis of disease.

73. (Withdrawn) The kit of claim 72, further comprising a third container holding an agent for digesting unhybridised RNA.

74. (Withdrawn) A kit comprising an array of nucleic acid molecules, at least one of which is a nucleic acid molecule according to claim 4.

75. (Withdrawn) A kit comprising one or more antibodies that bind to a polypeptide as recited in claim 1, and a reagent useful for the detection of a binding reaction between said antibody and said polypeptide.

76. (Withdrawn) A transgenic or knockout non-human animal that has been transformed to express higher, lower or absent levels of a polypeptide according to claim 1.

77. (Withdrawn) A method for screening for a compound effective to treat disease, by contacting a non-human transgenic animal according to claim 76 with a candidate compound and determining the effect of the compound on the disease of the animal.

78. (Currently Amended) An isolated polypeptide according to claim 1 (iii) which polypeptide is a fusion protein comprising a fragment which comprises or consists of the amino

acid sequence as recited in SEQ ID NO:20 or in SEQ ID NO:22 fused to a heterologous  
heterologous polypeptide.

79. (Cancelled) ~~An isolated polypeptide according to claim 1 (iii) which polypeptide is a fusion protein comprising a fragment which comprises or consists of a combination of the amino acid sequences as recited in SEQ ID NO:4 and SEQ ID NO:6 fused to a heterologous polypeptide.~~